Midterm Follow-up of *En-bloc* Kidney Transplantations from Deceased Pediatric Donors to Adult Recipients: A Case Series of a 6-Year Single-Center Experience

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ABSTRACT

Background: The organ shortage is the main concern for kidney transplantation. Using deceased pediatric donors either as single or in an *en-bloc* manner is one way to solve this problem. We reviewed 21 en-bloc pediatric deceased kidney transplantations to adult recipients.

Methods: From May 2010 to May 2016, 472 deceased kidney transplantations have been performed in our hospitals. Twenty-one of these were pediatric kidney transplantations to adult recipients (age < 5 years, kidney size < 8 cm, donor weight <15 kg). Follow-up (ranging from 3 to 36 months) included clinical findings and complications plus serial creatinine levels and kidney size with ultrasonography and dimercaptosuccinic acid renal scan.

Results: Among 21 patients, 52.4% were female. The mean age of participants was 28.85 ± 10.29 years. The preoperative mean size of the grafts was 6.94 ± 0.58 centimeters reaching 8.52 ± 0.98 and 10.20 ± 1.2 after 3 and 12 months of postoperative follow-up, respectively (P-value < 0.001). Means of serum creatinine was 1.61 ± 0.39, 1.45 ± 0.39, 1.32 ± 0.37, and 1.17 ± 0.28 mg/dl at postoperative 1, 3, and 6 and 12 months, respectively (P-value < 0.001). In a 12-month follow-up (range, 3 to 36 months), the complication-free rate was 61.9%, one-year patient survival was 90.5%, and one-year graft survival was 100%.

Conclusion: *En-bloc* pediatric deceased kidney transplantation is an acceptable alternative for adult recipients, with a great midterm patient and graft survival. Longer follow-up is recommended to assess their long-term outcomes.

KEYWORDS: Kidney transplantation; Pediatric donor; Deceased donor; Graft survival

INTRODUCTION

The organ shortage for kidney transplantation has been increasing in recent years [1, 2]. The number of candidates waiting for kidney transplantation has approximately doubled between 2002 and 2013, while 30% of them had been on dialysis for a long time [3]. It is demonstrated that this long waiting time on dialysis may strongly decrease both patient and graft survival following renal transplantation [4]. Different ways have been recommended to solve this problem, including using marginal kidneys from the elderly, as expanded criteria donors (ECD), and potential pediatric donors [5-7]. The use of pediatric kidneys for adult recipients either as single or *en-bloc* has been reviewed in dif-

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ferent studies [8-10]. Some studies showed an increased risk of complications and lower graft survival [8, 9], while others revealed similar survival between adult and pediatric donor kidneys [10]. In this study, we report our experience in *en-bloc* kidney transplantation from pediatric donors to adult recipients.

MATERIALS AND METHODS

Patients

In this cross-sectional study, we reviewed the results of our en-bloc kidney transplantations from May 2010 to May 2016. In this period, a total of 472 deceased kidney transplantations have been done in the Montaserieh transplantation center of Mashhad, Iran. Of those, 21 were *en-bloc* kidney transplantations from deceased pediatric donors. The inclusion criteria were donors with at least one of the following: less than five years of age, kidney size lower than 8 cm, and donor weight lower than 15 kilograms. The demographic characteristics of the recipients were recorded. Serum creatinine levels were measured at postoperative months 1, 3, 6, 9, and 12. Ultrasonography was performed at 3 and 12 months postoperatively to assess the anatomy and diethylenetriamine pentaacetic acid (DTPA) scan as needed to evaluate the function of the kidneys. Pre-operative assessment of bladder volume is helpful for patient selection for *en-bloc* transplantation because a small bladder decreases the surgeon's ability to provide tension-free anastomosis. Therefore, patients with long-duration anuria, previous bladder surgeries, neurogenic bladder, and patients with prior kidney transplantation are not suitable candidates for *en-bloc* kidney transplantation.

Surgical Technique

For the *en-bloc* procedure, both kidneys of the pediatric donors were harvested. The donors' aorta and inferior vena cava (IVC) were closed superior to the renal vessels. The infrarenal aorta and vena cava were used for anastomosis. Using a pararectal or Gibson incision on the harvested kidneys was positioned carefully in the extraperitoneal fossa. The donor's aorta was anastomosed via Prolene 4-0 suture to the recipient's aorta or external iliac artery, using the end-to-side technique. Likewise, the IVC of the donor is anastomosed to the patient's external iliac vein via the end-to-side technique. Absorbable monofilament sutures are not available in Iran. Therefore we anastomosed the vessels via Prolene 4-0 sutures in a continuous fashion. Ureteroneocystostomy was performed through the Wallace technique in 18 patients. Ureters in the other three patients were anastomosed separately from the bladder. After the anastomosis, a double-J stent was placed in each ureter for 4-6 weeks. The Urethral Foley catheter was removed on the 5th postoperative day. Postoperative recipient management: Mycophenolate mofetil, prednisolone, and cyclosporine immunosuppressive regimen were the same for all patients. Episodes of rejection were treated by anti-lymphocyte globulin and pulse steroid therapy.

Ethical consideration

The ethics committee of Mashhad University of Medical Sciences approved the method of this study under the code: IR.MUMS.fm.REC.1396.818.

Statistical Analysis

We used the Spearman rank correlation, Wilcoxon signed-rank test, and Kaplan-Meier method to assess and determine the relationship between variables, pre- and post-transplantation size of the kidneys, and patient graft survival, respectively. To analyze our data, we used SPSS software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 16.0. Armonk, NY: IBM Corp). P-values of less than 0.05 were considered significant.

RESULTS

Of 21 donors, 13 (62%) were male. The mean age of donors was two years, ranging from six months to four years. The mean weight was 9.25 (range 4-12) kilograms. All donors were brain-dead. We did not use the preservation machine because both donors and recipients were in the same center. Cold ischemia time was 45 to 60 minutes.

Table 1: Demographic characteristics of recipients (* deaths are not considered complication because they were due to other medical conditions).

Recipient number	Age	Follow-up duration	Complication
1	36.0	3.0	(Died*)
2	20.0	6.0	(Died*)
3	18.0	9.0	
4	36.0	9.0	
5	39.0	9.0	Acute Tubular Necrosis
6	26.0	10.0	Renal vein thrombosis
7	39.0	10.0	
8	40.0	10.0	
9	24.0	11.0	Ureteral stenosis
10	21.0	11.0	
11	19.0	12.0	
12	37.0	12.0	Lymphorrhea
13	19.0	12.0	
14	21.0	12.0	Ureteral stenosis
15	18.0	12.0	
16	34.0	12.0	Subcutaneous hematoma
17	21.0	13.0	
18	19.0	13.0	
19	54.0	16.0	Acute Tubular Necrosis
20	24.0	20.0	
21	41.0	36.0	Lymphorrhea

Of 21 recipients, 10 (47.6%) were male and 11 (52.4%) were female. The mean ± SD age of the recipients was 28.85 ± 10.36 years. In 19 cases, donors' aorta and vena cava were anastomosed to the external iliac vessels. In 2 other patients, anastomosis was made to the vena cava and aorta of the recipients. In 18 patients Wallace technique was used for ureteral anastomosis, and in 3 patients, separate ureteral anastomosis with the Lich technique was carried out.

The mean ± SD of serum creatinine was 1.61 ± 0.39 mg/dl at the first month post-operatively reached 1.45 ± 0.39, 1.32 ± 0.37, and 1.17 ± 0.28 at 3, 6, and 12 months, respectively. The p-value for the trend and in each multiple comparison was less than 0.001 (Table 1). There was no significant correlation between the mean difference of creatinine in 12 months follow-up and the age and sex of the patients (P-value: 0.45 and 0.98, respectively).

The mean ± SD size of the grafts was 6.94 ± 0.58 centimeters preoperatively by ultrasonography that reached 8.52 ± 0.98 and 10.20 ± 1.2 after 3- and 12-months' postoperative follow-up, respectively. The p-value for the trend and in each multiple comparison was less than 0.001 (Table 2). There was no significant difference between the mean size of the grafts in male and female patients before surgery and after 12-month follow-up (7.10 and 6.80 preoperatively to 10.29 and 10.11 after 12 months in male and female recipients, respectively. P-value: 0.25 and 0.75) (Table 3). The median follow-up duration was 12 months, ranging from 3 (patient death) to 36 months. DTPA scan was performed between 6 to 18 months following the transplantation. DTPA for all cases showed normal perfusion and

Table 2: Mean creatinine levels of the recipients.

Month	Creatinine					
	Mean (median)	SD	Range	95% Confidence interval		P-value
				Lower Bound	Upper Bound	
1	1.61 (1.40)	0.39	1.29 – 2.8	1.452	1.837	<0.001
3	1.45 (1.37)	0.39	1.18 – 1.85	1.274	1.663	
6	1.32 (1.30)	0.37	1.05 – 1.80	1.157	1.482	
12	1.17 (1.22)	0.28	0.95 – 1.46	1.036	1.322	

function of the transplanted kidneys. Three of the reports detected a mild dilatation in the upper kidney with no obstruction (Figure 1).

In a 12-month follow-up, complications included acute tubular necrosis in 2 patients (10.5%), which was managed conservatively. Ureteral stenosis in 2 (10.5%), renal vein thrombosis in 1 (5.25%), subcutaneous hematoma in 1 (5.25%), and lymphorrhea in 2 (10.5%). We had no episodes of rejection. The complication-free rate was 61.9%. We had two cases of ureteral stenosis that were managed and saved by ureteral reimplantation. Wallace was the technique of primary anastomosis in both. We used the Lich technique for reimplantation in both cases, and each ureter was reimplanted separately. The renal vein thrombosis occurred ten days after transplantation. Gross hematuria was the presenting symptom, and the kidney was saved by immediate anticoagulation therapy. Furthermore, two deaths with functioning grafts occurred due to myocardial infarction and motor-vehicle accidents 3 and 6 months following surgery, respectively. One-year patient survival was 90.5%, and since none of the grafts were lost independent of death, one-year graft survival was 100% (Figure 2).

DISCUSSION

Standard criteria donors cannot supply the demand for organs for a kidney transplant. The deceased pediatric donors are one way to overcome this organ shortage [11-13]. Technical difficulties, higher vascular complications, lower nephron mass, development of hyper-filtration injury, increased risk of rejection, and difficulties in immunosuppressive therapy are some problems with pediatric deceased kidney donation [14-17].

The results of some studies are against the use of pediatric kidney donors. In the study of Neyumayer *et al.* graft survival was significantly worse in patients receiving grafts from younger than ten years compared to older donors. Also, comparing patients with donor grafts aged ≤ 5 or 6-10 years showed a further adverse age-related effect [9]. Bresnahan *et al.* showed poorer graft survival in pediatric do

Table 3: Mean graft sizes of the recipients.

Month	Graft size (Cm)					
	Mean (median)	SD	Range	95% Confidence interval		P-value
				Lower Bound	Upper Bound	
0	6.943 (6.90)	0.58	6.10 – 7.50	6.677	7.209	<0.001
3	8.524 (8.30)	0.98	7.40 – 10.80	8.076	8.971	
12	10.200 (9.90)	1.2	8.70 – 11.10	9.649	10.751	

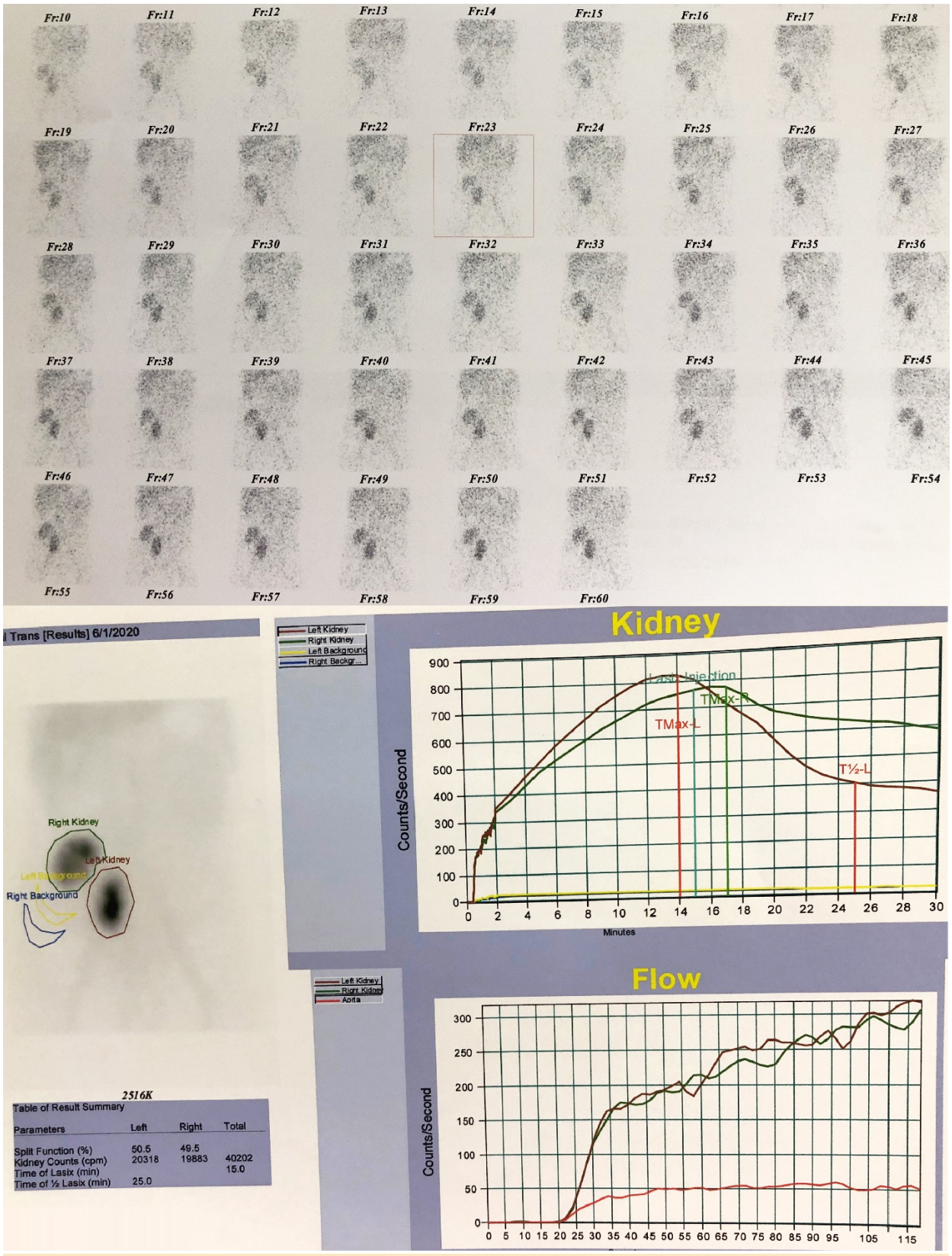

Figure 1: DTPA scan reported mild dilatation of the superior kidney without obstruction. Function and perfusion of both kidneys were reported normal. (DTPA: diethylenetriamine pentaacetic acid)

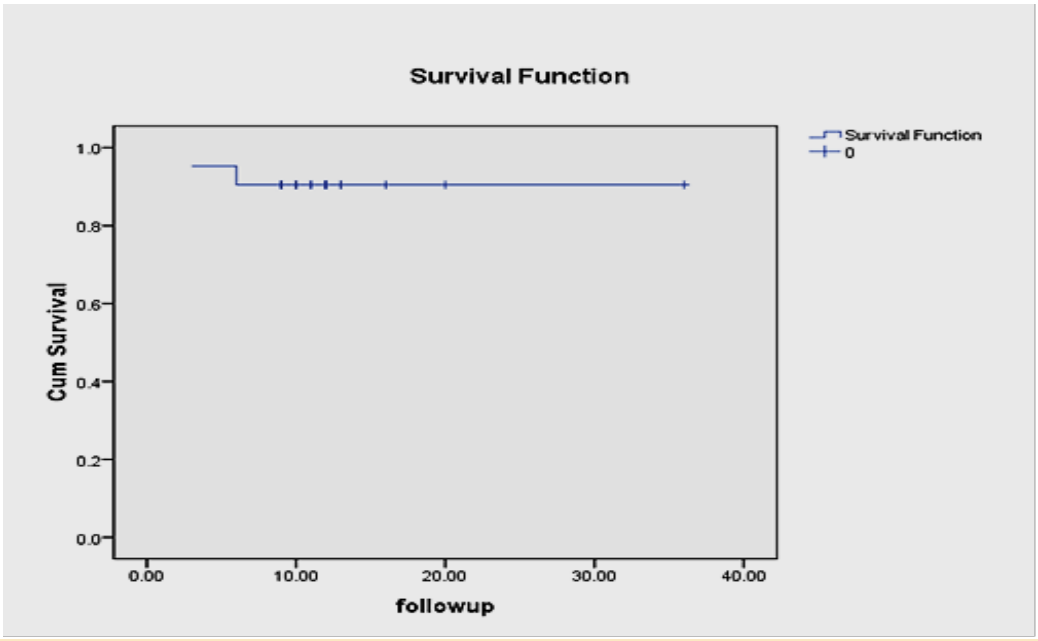

Figure 1: Kaplan-Meier curve shows patient survival and follow-up duration (2 deaths at the third and sixth month of follow-up).

nor transplants. They also reported a progressive increase in donor age was associated with improved graft survival when the donors were 6-11 years [18]. Also, in the study by Harmon *et al.* the risk of graft loss was related to donor age. The risk of graft loss from a neonate donor was 2.7-fold that of the ideal donor. Additionally, they showed that 9.9% of grafts from donors less than or equal to 5 years of age were lost due to vascular thrombosis, primary non-function, and other technical causes, compared with 4.6% in 6-9, 4.4% in 10-39, and 2.8% is greater than or equal to 40-year-old donors [19]. Drakopoulos *et al.* showed that the survival rate of patients who received a kidney from less than 6-year donors was lower than older donors [8].

Some studies showed favorable results of transplants from pediatric donors in recent years, both with single or *en-bloc* transplants. Single renal transplants allow each graft to be transplanted into different recipients which increases organ utilization; however, the outcomes remain controversial. Although some studies showed no difference between single and *en-bloc* transplants [20], a recent meta-analysis showed that patients who received en-bloc kidney transplantation were more likely to have better graft survival [6]. The sample sizes of the studies that are in favor of pediatric donors are relatively small. Mahdavi *et al.* reported seven patients with both one-year graft and patient survival of 85.7% [21]. Beasley and colleagues reported 16 *en-bloc* kidney transplantations with 94% graft survival after three years. They reported the following complications: 2 deaths secondary to infectious and cardiac problems, 7 cases of acute rejection treated with anti-lymphocyte antibody and steroid, 4 cases of ureteral strictures managed by reimplantation, and one lymphocele [22]. El-sheikh *et al.* reported 15 *en-bloc* pediatric deceased kidney transplantation with one-year graft survival of 92.8% and patient survival of 100%, and they only reported one case of lymphocele [23].

The most important aspect of the surgery is the positioning of the kidneys so that the ureters reach the bladder with no tension. Furthermore, the positioning should provide the least possibility of torsion or kink of the vessels. Considering patient selection criteria and surgical techniques which were discussed in the methods, none of these patients required ureteral reconstruction procedures like blad-

der patch or Boari flap.

We also showed a significant increase in the size of transplanted kidneys confirmed by ultrasonography. Merkel has reported similar findings, they showed that the size of *en-bloc* transplanted kidneys would be doubled within the first two to three weeks, and at 18 months postoperatively, they would reach the adults' size [24].

The main limitation of this study is its small sample size and retrospective nature. Moreover, we were not able to calculate patients' GFR accurately due to weight variations. However, our study is strong as it included homogenous patients who underwent standardized surgery by a highly skilled transplant team in an academic center.

In conclusion, *en-bloc* kidney transplantation from deceased pediatric donors is suitable for adult recipients. One-year patient and graft survival are acceptable with a low complication rate. Meticulous attention to clinical, laboratory and imaging findings is essential. Hematuria due to vein thrombosis needs immediate evaluation. To reduce ureteral stenosis, separate ureteral anastomosis is preferred. Prospective studies with larger series and longer follow-ups are needed to confirm these findings.

CONFLICTS OF INTEREST: None declared.

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